Rejection under 35 U.S.C. § 103(a)

Claims 17, 19 and 21-27 have been newly rejected as unpatentable over U.S. Pat. No. 6,066,718 (Hardman et al.) in view of Whittington et al. and U.S. Pat. No. 6,468,547 (Buchsbaum et al.).

The Office asserts that Hardman et al. teach that anti-IgE antibodies can be used to treat or prevent allergic diseases *in vivo* and that "Whittington supplements Hardman by teaching the intravenous delivery of an adenoviral vector encoding a single chain antibody *in vivo* resulting in the expression of biologically active levels of encoded antibody." Office Action at pg. 5). The Office asserts that Buchsbaum further supplements Hardman and Whittington by teaching the therapeutic use of adenoviral vectors to express single chain antibodies . . . *in vivo* to treat disease." (Office Action at page 6). The Office admits that Hardman does not teach the use of nucleic acid encoding an anti-IgE antibody *in vivo*. Further, the Office asserts that "Hardman does teach *in vivo* methods of administering anti-IgE antibodies" merely by their administration to a patient. Applicants respectfully traverse this rejection.

As the Office knows, the requirements for establishing a *prima facie* case of obviousness requires some teaching, suggestion, or motivation in the references themselves to modify those prior art teachings to arrive at the claimed invention. In addition, the Office cannot rely on the Applicants' specification as a blueprint to choose teachings that appear to suggest the claimed invention. Those references must be examined as a whole for everything they teach.

In *In re Fine* the claims were directed to a system of detecting and measuring minute quantities of nitrogen compounds comprising a gas chromatograph, a converter which converts nitrogen compounds to nitric oxide, and a nitric oxide detector. The primary reference disclosed a system for monitoring sulfur compounds and the secondary reference taught a nitric oxide detector. The Examiner asserted that it would have been within the skill of the art to substitute one type of detector for another. The Court reversed finding no support for such a conclusion.

Such is the case here. The Office is asserting that it would have been obvious to substitute the anti-IgE antibody of Hardman for the fusion protein of Whittington or the anti-cancer erbB-2 of Buchsbaum. However, there is no suggestion in either reference that other types of targets other than directed cancer targets can be used. All of the examples in both of the secondary references are cancer related targets. There is no support for a conclusion that it would have been obvious to substitute an antibody to a totally unrelated, non-analogous field, in this case IgE-mediated allergic diseases.

Moreover, the reference that the Office relies on to teach the therapeutic expression does not say "biologically active levels of encoded antibody" as the Office asserts, but rather it states "cells infected with the adenoviruses both *in vitro* and *in vivo* produce bioactive **fusion protein** at therapeutic levels". The teachings of Whittington are directed to an antibody fused to a cytokine and the cytokine is the active element of the invention. There is no suggestion in this reference to eliminate the fused bioactive element of the construct and use only

the scFv. Indeed, the Courts have stated that the elimination of an element of the prior art invention and retaining a similar function is the quintessential case of nonobviousness. In a related aspect to this discussion, if the proposed modification to the prior art would change the principle of operation of the prior art invention being modified, then the teaching of that reference is not sufficent to render the claims *prima facie* obvious (*In re Ratti* , 123 USPQ 349 (CCPA 1959), See MPEP 2143.01). Here, the modification of the prior art to remove the fused element (the cytokine) changes the principle of operation of Whittington's teaching. His invention was merely using the antibody to target an active element to a specific cell type. The fact that he used an adenovirus vehicle does not change the nature of his invention.

In view of the foregoing remarks, Applicants submit that the Office has not met its burden of establishing a *prima facie* case of obviousness and therefore, request that the rejection be withdrawn.

Conclusion

Applicants submit that the claims are in condition for allowance and request Notice of same.

Respectfully Submitted,

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